REMARKS/ARGUMENTS

The claims are 1-8 and 10-12, which have been rejected on the basis of the prior art. Specifically, claims 1-3, 5 and 10-12 were rejected under 35 U.S.C. 103(a) as being unpatentable over *Ogura et al. U.S. Patent No. 6,702,754* in view of *Hood, Jr. et al. U.S. Patent No. 5,680,870* and *Cohn et al. U.S. Patent No. 5,054,493*. The remaining claims were rejected under 35 U.S.C. 103(a) as being upatentable over *Ogura et al. '754, Hood, Jr. et al., Cohn et al.* and further in view of *Ogura U.S. Patent No. 7,029,449* (claim 4), *Bui et al. U.S. Patent No. 6,398,727* (claims 6 and 7), or *Gallant et al. U.S. Patent No. 5,238,001* (claim 8).

Essentially the Examiner's position was that *Ogura et al. '754* discloses the apparatus and method recited in the claims, except for features which were said to be shown by the secondary references to *Hood, Jr. et al., Cohn et al., Ogura '449, Bui et al. or Gallant et al.*

This rejection is repsectfully traversed.

As set forth in claim 1, Applicants' invention provides an apparatus for measuring hemodynamic parameters by non-invasive, cuff based occlusive, blood pressure measurement. The apparatus includes occlusive, oscillometric automatic blood pressure meter and units, determining the values of hemodynamic parameters, including an oscillation wave separating and storing signal detector, a digital anti-filter to compensate the distortions rising at the sampling, separating and digitizing the oscillation wave, an amplitude arithmetic unit establishing an Augmentation Index (Aix), and a synthesizing unit establishing an Ejection Duration (ED). The sampling rate of the oscillation wave separating and storing signals detector is at least 200/heart cycle; the storage unit resolution thereof being organized at least nine bit.

As set forth in claim 12, Applicants' invention provides a method for non-invasive measurement of hemodynamic characteristics including the steps of performing a standard stepwise blood pressure measurement using an occlusive, pressure-sensor cuff placed on the brachial artery, storing systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate

(HR) values, subsequently setting the cuff to supra-systolic pressure range over the systolic pressure, performing a pressure oscillometric pulse wave detection at supra-systolic pressure range, receiving oscillation curve and simultaneously by an "anti-filter" process compensating for signal distortions appearing at sampling, calculating an Augmentation Index (Aix) on the basis of the wave amplitudes from the oscillation curves so received; and calculating the Ejection Duration (ED) value on the oscillating curve determining the minimum point after the first reflex wave.

Applicants believe it would be helpful for the Examiner to consider the various types of devices and methods for the assessment of arterio/atherosclerosis and to that end, attached hereto are illustrative pictures 1-4 for explanation purposes.

The devices and methods directed to the assessment of arterio/atherosclerosis can be sorted into essentially different groups of theoretically and practically different technical and medical-technical circumstances (see Picture 1 attached). The

first two big groups are the **invasive** and the **non-invasive** ones. See Applicants' disclosure at page 1, lines 20 and 25. Applicants' method and apparatus as recited in claims 1 and 12 are directed to non-invasive methods.

The non-invasive apparatuses may be equipped with a **contact pressure sensor**, or with only an **air-filled upper arm cuff**. The differences between these devices are discussed at page 1, lines 25-30, page 7, line 22-24 and page 11, lines 12-17 of the disclosure. Applicants' method and apparatus as recited in claims 1 and 12 use a cuff as a sensor on the upper arm. See Picture 1.

Cohn et al. concerns high-blood-pressure examination with a catheter, i.e. an **invasive** method (Class 1.1 as in Picture 1). *Hood, Jr. et al.* concerns **blood pressure measuring** with a cuff (1.2.1 in Picture 1). *Ogura et al.* '*754* and *Ogura* '*449* concern arterio/atherosclerosis examination **with a contact sensor**, supplied with a cuff for measuring blood pressure (combination of classes 1.2.2.1 and 1.2.1).

Also known is *Ogura et al. U.S. Patent No. 6,712.768* cited in the disclosure at page 2, lines 14-20 and page 4, lines 19-28. *Ogura et al. '768* concerns measuring of hemodynamic data with a cuff sensor.

The above-mentioned devices and methods differ from Applicants' apparatus and method as recited in claims 1 and 12 because they concern different objects or purposes or use a different applied sensor. Only *Ogura et al. '754* and *Ogura '449* are directed to measuring hemodynamic parameters, but they use a contact pressure sensor, specifically on the neck of the patient. The cuff is used only supplementarily for the blood pressure measurement. As can be seen in FIG. 6. of *Ogura et al. '754*, the cuff is connected only to the blood pressure determining means. See Picture 2 attached, which is a modified/slightly enlarged representation of FIG. 6 of *Ogura et al. '754* with the relevant parts separated and highlighted. The blood pressure determining means of *Ogura et al. '754* determines systolic, diastolic and mean blood pressure values in the common oscillometric way. **Unit 86 feeds only these three values to the displaying means.** See

Ogura et al. '*754* at column 7, lines 22-31. For obtaining a good quality recording of a pressure pulse wave, the sensor array positioned on the neck has to be pushed against the carotid artery with a determined moderate pressing force, which deforms (***applanates***) but does not occlude the artery, i.e. it is not a suprasystolé measuring. See Picture 3 attached.

This procedure, however, not only might be quite inconvenient for the patient but also is a source of risk as it disturbs the cerebral blood circulation due to the occlusion of the low pressure veins of the neck partially or completely blocking the return flow from the brain towards the heart. The measuring procedure published in *Ogura et al.* '*754* and *Ogura* '*449* is known as ***applanation tonometry*** in the medical field. The basic principle of this method is completely different from the one of the oscillometric method. See Applicants' disclosure at page 1, lines 25-30, page 7, lines 22-24 and page 11, lines 12-17. The point of the applanation tonometry method is to deform the artery wall with an array of sensors for making it stress-free (decreasing the intramural pressure of the arterial wall in order to eliminate its local behavior from the examination). By doing

so, the characteristics of the arterial wall do not influence the measurement, and the pressure sensors measure the arterial pulse wave directly as a pressure signal. Moreover, the blood flow is maintained during the whole cardiac cycle. See Picture 4 attached.

With Applicants' apparatus and method as recited in claims 1 and 12, the cuff is used both as a sensor and as a pressing means. A main aspect of Applicants' apparatus and method is that the majority of the hemodynamic parameters are measured on suprasystolic pressure, i.e. the blood flow is entirely stopped and the artery is completely occluded. This feature cannot be carried out in the case of *Ogura et al '754* and *Ogura '449*, as doing so would cause the excessive limitation of the cerebral circulation not only for the venous circulation but also for the arterial circulation as well. By the cuff, only volume changes can be detected directly, which is the basic principle behind oscillometry. These volume changes are generated by the displacement of the arterial wall due to arterial pressure changes. It is the volume change of the air in the cuff that

shifts into pressure change (oscillation) because of the closed chamber.

Applicants have recognized that oscillations of the cuff during blood pressure measurement carry much more information than its maximum value. They have found that these pressure changes at suprasystole (i.e. when brachial blood flow is entirely stopped) are practically identical to the intraarterial pressure waveforms, using appropriate signal correction. For recording these minor pressure changes (recorded at suprasystolic cuff pressure), a high resolution signal processing is needed. In the prior art, the suprasystolic cuff oscillations were considered to be useless (except for *Ogura et al '768*) and were not recorded but rather were deleted to save computing time and storage.

In view of the above, and as the Examiner has recognized, Applicants' apparatus and method as recited in claims 1 and 12 are clearly novel. It is respectfully submitted, moreover, that Applicants' apparatus and method are likewise not rendered

obvious by any of the cited references whether considered alone or in combination for the following reasons.

Contrary to the Examiner's position, it is respectfully submitted that it would not have been obvious to apply the high resolution methods of *Cohn et al.* and *Hood, Jr. et al.* in the arterio/atherosclerosis examination of *Ogura et al. '754*. In 1991, *Cohn et al.* used 200 samples/sec and 12-bit signal processing in order to receive higher resolution; however, this procedure is performed on an invasively measured signal. Furthermore, this signal is not analyzed but rather is used as the outcome of a mathematical equation for optimizing its parameters. A significant difference from Applicants' apparatus and method as recited in claims 1 and 12 is that by an invasive measurement, **analog** signal separation (i.e. an RC-unit) is not needed as there is no static pressure component in the measured signal. Therefore, there is no need for any correction of the analog distortion. Considering the above, it is respectfully submitted that the signal acquisition units differ significantly by the two methods as well as the further signal processing algorithms.

Hood, Jr. et al. is no more relevant. In 1997, *Hood, Jr. et al.* did not use *Cohn et al.'s* methods. Instead, *Hood, Jr. et al.* used a transformation with a 14-20-bit A/D unit. In *Hood, Jr. et al.'s* application, the pulse signal is separated digitally. The problem in this case is that the dynamic component (oscillations) is one-two orders of magnitude smaller than the static one. To be able to record these oscillations with a sufficiently good quality, a high resolution is needed. At the traditional blood pressure measurement, the high resolution is necessary in order to find exactly the top of the cuff oscillations (i.e. the size of maximum amplitudes) in each heartbeat. The distortion of signals occurring at the sampling does not disturb the results of the blood pressure measurement -- systolic and diastolic blood pressure (SBP, DBP), and heart rate (HR), -- but it certainly causes significant errors during the arterio/atherosclerosis examination -- augmentation index (Aix), ejection duration (ED), pulse wave velocity (PWV), -- where it is necessary to determine not only the maximum amplitudes, but also the whole oscillation waveform with high resolution which represents the blood pressure waveform.

The aim of *Hood, Jr. et al.'s* application is to eliminate the analog signal separation unit (RC-unit) in order to simplify both the hardware and software. See *Hood, Jr. et al.* at column 3, lines 40-61. For this purpose, *Hood, Jr. et al.* suggests two preferred embodiments -- which are therefore not equipped with an RC-unit -- one with a high resolution (14-20 bit) A/D conversion and another with a smaller resolution (8-bit) digitalization supplied with a dither signal and an FIR filter to reach adequate quality. Thus, *Hood, Jr. et al.* does not deal with analog signal distortions.

Consequently, it is respectfully submitted that it is not possible to use the methods "per se", which are known and used in blood pressure measuring for arterio/atherosclerosis examination without additional technical innovative steps. Thus, it is respectfully submitted the prior art of measuring blood pressure fails to provide sufficient guidance to one skilled in the art to create an effective arterio/atherosclerosis examining device and method according to clinical requirements without some inventive step.

In addition, **the "anti-filter"** used in Applicants' apparatus and method as recited in claims 1 and 12 is quite different from *Hood, Jr. et al.'s* dither signal and FIR filter method, from the viewpoint of its theoretic base, its object, and the used proceeding. *Hood, Jr. et al.'s* method aims to carry out an A/D conversion of sufficient quality without applying a more expensive high bit-resolution A/D converter. Consequently, *Hood, Jr. et al.* improves the digital errors appearing at the digitalizing step of the A/D converter. In *Hood, Jr. et al.'s* method, the received signal is mixed with a "dither signal" of an outer source (See Wikipedia's definition of Dither). The digitization is carried out on this mixed signal. Before the evaluation the two signals are separated with a "per se" known FIR frequency filtering (low-pass filter).

In Applicants' apparatus and method as recited in claims 1 and 12, the "anti-filter" compensates the analog distortions arising at the separation of the original signal to AC and DC components on the RC-unit. Applicants' method does not use any kind of foreign signal, and/or mix the original signal with a vice-signal, or the like. It is respectfully submitted that the

difference between Applicants' method and the method recited in *Hood, Jr. et al.* is readily apparent.

The applied anti filter in Applicants' invention is a special application of "mathematical filtering". With Applicants' apparatus and method as recited in claims 1 and 12, the distortions arising at the analog signal separation can successfully be compensated with the demonstrated software process (See Applicants' FIG. 5), with the optimized parameters determined empirically.

In the methods of *Ogura et al '754*, it would be necessary to know the true wave picture as good as possible, although because of the essentially different signal acquisition of the carotid tonometry there is no need for compensating analog errors. In *Ogura et al. '768*, one sees that in the suprasystolic range only the time shift of the waves is determined. The amplitude values for the augmentation index are determined in a next step in the diastolic range. This process causes problems, not only because two steps are needed instead of one, but also because in the diastolic range the pressure is significantly different due to

the blood flow. See Applicants' disclosure at page 2, lines 14-20, page 4, lines 19-28, page 11, lines 27-31, page 12, lines 1-2 and page 13, lines 25-31.

It is very important to know the complete pressure wave picture for the determination of hemodynamic parameters in the arterio/atherosclerosis examination. See Applicants' disclosure at page 12, line 25 to page 13, line 2 and FIGS. 3-4.

As discussed in the disclosure, the pulse wave picture is very variable. FIGS. 3 and 4 show two typical variants representing the two ends of the pulse wave picture scale. In the everyday physician practice, one may meet with all variants in the range. It is very important always to determine the hemodynamic parameters according to the actual variant. Consequently, for the correct evaluation, for the right diagnosis and the right therapy, one must know the true type of the received oscillogram, which may be realized only by applying together all features of Applicants' apparatus and method as recited in claims 1 and 12. The wave pictures in FIG. 5 of *Ogura et al* '754: wc, wi, wr, are the components of the same one wave

type. See Applicants' FIG. 3. Beside those components, the variants of the other type (see Applicants' FIG. 4) and the transitional forms between those two major types present most of the cases. The received information allows physicians to be able to evaluate the arterio/atherosclerotic status. If the actual wave picture is determined wrongly at the hemodynamic parameters examination, the actions based on this information may also be false, perhaps even harmful.

With Applicants' apparatus and method as recited in claims 1 and 12, it is possible to determine the Aix, ED, PWV in one step, avoiding the complications of the *Ogura/Colin et al. '768* method, wherein in a first step, above the systolic pressure, only the time shift is determined, and in order to calculate the Aix and other parameters this time shift is projected on the received diastolic oscillogram in a second step.

Applicants have found that the hemodynamic characteristics may be determined with the use of a simple cuff only if one knows the correct type of actual oscillogram, which is possible only if one receives an oscillogram with satisfactory resolution and with

compensation of the signal distortions rising at the sampling. Consequently, it is respectfully submitted that the features of Applicants' apparatus and method may not be considered separately, but rather must be considered in their entirety as a combination. It is respectfully submitted that the prior art fails to provide any disclosure or suggestion sufficient to direct one skilled in the art to create an effective cuff-based arterio/atherosclerosis examining device and method according to clinical requirements and that the advantageous result achieved from Applicants' apparatus and method as recited in claims 1 and 12 was entirely unexpected.

The remaining references cited by the Examiner with respect to the dependent claims, namely *Bui et al.* and *Gallant et al.* have been considered, but are believed to be no more relevant. None of these references discloses or suggests an apparatus or method as recited in Applicants' claims 1 and 12 that has the combination of structure and steps recited in the respective claims or teach the benefits that are achieved by that combination.

Accordingly, it is respectfully submitted that claims 1 and 12, together with claims 2-8 and 10-11 which depend directly or indirectly thereon respectively, contain patentable and unobvious subject matter.

In view of the foregoing, withdrawal of the Final Office Action and allowance of this application are respectfully requested.

Respectfully submitted,
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Enclosures: Pictures 1-4

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